CLAIMS

1. An assay method for TSH-R auto-antibodies or TSH, which method includes the step (a), which is:
contacting a test sample, in the presence or absence of TSH, with cells from a clone expressing human TSH-R stably transfected with a reporter construct comprising cDNA of both
(i) a reactant, such as an enzyme, capable of causing a measurable response when brought into contact with a corresponding substrate, such as a protein, and
(ii) a promoter containing cyclic AMP (cAMP) response elements (CREs),
whereby levels of the reactant vary with induced endogenous cAMP levels.

2. An assay method according to claim 1, wherein the promoter comprises a promoter sequence or synthetic oligonucleotide which contains the CRE consensus sequence, TGACGTCA.

3. An assay method according to claim 1 or claim 2, further including the step (b), which is:
adding the corresponding substrate to cells thus contacted.

4. An assay method according to claim 3, further including the steps:
(c) measuring the response in the cells exposed to the substrate; and
(d) comparing the response from test step (c) with the response from a standard or normal sample which has undergone steps (a) to (c).

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5. An assay method according to any preceding claim, wherein the promoter is that for the glycoprotein hormone alpha subunit that contains tandem cAMP response elements.

6. An assay method according to any of claims 1 to 4, wherein the promoter comprises a construct driving the CAT enzyme

7. An assay method according to any preceding claim, in which the measurable response is a colour change, fluorescence change or emission of light.

8. An assay method according to claim 7, wherein the reactant is selected from chloramphenicol acetyl transferase (CAT), Firefly luciferase, Renilla luciferase, β-galactosidase, alkaline phosphatase, horseradish peroxidase and green fluorescent protein.

9. An assay method according to claim 4, which comprises, in step (a), the use of a luciferase cDNA driven by a promoter containing cAMP response elements; in step (b), the use of luciferin; and, in step (c), measuring the light output from the cell lysate in the presence of luciferin.

10. An assay method according to any preceding claim, wherein the reporter construct comprises α-luciferase.

11. An assay method according to any preceding claim, wherein the clone for use in step (a) is obtainable by stable co-transfection of CHO cells or any eukaryotic cell line with a cDNA containing the coding region of hTSH-R in a eukaryotic expression vector and a cDNA containing the reporter construct comprising both the promoter and the reactant.

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12. An assay method according to any preceding claim, wherein all reagents used therein are brought together in one or more steps; and/or wherein two or more of the steps (a) to (d) are carried out substantially simultaneously.

13. An assay method according to any preceding claim, which is carried out by manual, partly automated or fully automated means.

14. A kit for carrying out an assay according to any preceding claim.

15. A kit according to claim 14, which kit comprises:

(a) cells from a clone expressing human TSH-R stably transfected with a reporter construct comprising cDNA of both a reactant, such as an enzyme, capable of causing a measurable response when brought into contact with a corresponding substrate, such as a protein, and a promoter containing cyclic AMP (cAMP) response elements (CREs), whereby levels of the reactant vary with induced endogenous cAMP levels;

(b) a standard or normal sample for the assay;

(c) medium for culturing and/or reconstituting the cells; and

(d) instructions for carrying out the assay.

16. A kit according to claim 15, wherein the promoter comprises a promoter sequence or synthetic oligonucleotide which contains the CRE consensus sequence, TGACGTCA.

17. A kit according to claim 15 or claim 16, further comprising:

(e) buffer for lysing the cells; and/or

(f) buffer for the reporter construct, preferably luciferase buffer;

and/or

(g) corresponding substrate, preferably luciferin, in buffer; and, optionally, a luminometer.

18. A kit according to any of claims 14 to 17, wherein the reporter construct comprises the plasmid pA3luc having the glycoprotein hormone α subunit promoter introduced therein.

19. A kit according to any of claims 14 to 18, wherein the CRE-containing sequence is sub-cloned into a commercially-available luciferase reporter system, such as pGEM-luc.

20. A kit according to any of claims 14 to 18, wherein the reporter construct comprises a plurality of plasmids.

21. A kit according to any of claims 14 to 18, wherein the human TSH-R is sub-cloned into a eukaryotic expression vector.

22. A kit according to claim 21, wherein said eukaryotic expression vector is pSVL.

23. A kit according to claim 21, wherein the TSH-R is sub-cloned into a dual vector that incorporates the antibiotic resistance gene within the same plasmid.

24. A kit according to claim 23, wherein the dual vector comprises pcDNAIII.

25. A kit according to any of claims 14 to 24, wherein the cells for component (a) are from clone JP09 as identified herein, which have

been stably transfected with, in the order of, 10^5 TSH-R per cell.

26. A kit according to claim 25, wherein said cells are co-transfected with both α-luciferase cDNA and a puromycin resistance encoding plasmid.

27. A kit according to any of claims 14 to 26, wherein the cells are lyophilised (freeze-dried), frozen or comprised in a gel, and provided in individual containers.

28. A kit according to any of claims 14 to 26, wherein said cells are further co-transfected to provide the assay with a method of correcting for the number of cells seeded in a well during use.

29. A kit according to claim 28, wherein said cells are further co-transfected using a Renilla luciferase plasmid.

30. An assay method or a kit according to any preceding claim for use in association with a condition or disease selected from: autoimmune thyroid disease, non-autoimmune thyroid disease, autoimmunity of non-thyroid origin and polyendocrine disease.

31. An assay method or a kit according to any preceding claim for use in screening patients selected from: pregnant women, those with euthyroid eye disease, and those receiving amiodarone and/or lithium.

32. An assay method or kit according to any preceding claim for measuring TSAb or TBAb, or for measuring auto-antibodies to the TSH-R having part of its sequence modified, such as by having one or more of its amino acids replaced or otherwise modified to include tags.

33. Use of a reporter construct comprising cDNA of both
(i) a reactant, such as an enzyme, capable of causing a measurable response when brought into contact with a corresponding substrate, such as a protein
and
(ii) a promoter containing cAMP response elements (CREs),
whereby levels of the reactant vary with induced endogenous cAMP levels, which use is in an assay method or in the preparation of a kit, characterised in that said assay or kit is as defined in any preceding claim.

34. A use according to claim 33, wherein the promoter comprises a promoter sequence or synthetic oligonucleotide which contains the CRE consensus sequence, TGACGTCA.

35. A use according to claim 33 or claim 34, wherein the reactant enzyme is a luciferase and/or the substrate is luciferin.

36. A clone expressing human TSH-R stably transfected with a reporter construct comprising cDNA of both
(i) a reactant, such as an enzyme, capable of causing a measurable response when brought into contact with a corresponding substrate, such as a protein
and
(ii) a promoter containing cAMP response elements (CREs),
whereby levels of the reactant vary with induced endogenous cAMP levels.

37. A clone according to claim 36, wherein the promoter comprises a promoter sequence or synthetic oligonucleotide which contains the

CRE consensus sequence, TGACGTCA.

38. A clone according to claim 36 or claim 37, wherein the reactant enzyme is a luciferase and/or the substrate is luciferin.

39. Cells produced by a clone according to any of claims 36 to 38.

40. cDNA or mRNA expressing human TSH-R stably transfected with a reporter construct comprising cDNA of both
(i) a reactant, such as an enzyme, capable of causing a measurable response when brought into contact with a corresponding substrate, such as a protein
and
(ii) a promoter containing cAMP response elements (CREs),
whereby levels of the reactant vary with induced endogenous cAMP levels.

41. cDNA or mRNA according to claim 40, wherein the promoter comprises a promoter sequence or synthetic oligonucleotide which contains the CRE consensus sequence, TGACGTCA.

42. cDNA or mRNA according to claim 40 or claim 41, wherein the reactant enzyme is a luciferase and/or the substrate is luciferin.

43. Human TSH-R stably transfected with a reporter construct comprising cDNA of both a reactant, such as an enzyme, capable of causing a measurable response when brought into contact with a corresponding substrate, such as a protein, and a promoter containing CRE.